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Predicted contribution of folic acid fortification of corn masa flour to the usual folic acid intake for the US population: National Health and Nutrition Examination Survey 2001–2004

Abstract

Background: Folic acid can prevent up to 70% of neural tube defects (NTDs) if taken before pregnancy. Compared with other race-ethnicities, Hispanic women have higher rates of NTDs, lower rates of folic acid supplement use, and lower total folic acid intakes. **Objective:** The objective was to assess potential effects of fortifying corn masa flour with folic acid on Mexican American women and other segments of the US population. **Design:** A model was developed by using data from the National Health and Nutrition Examination Survey 2001-2004 to estimate the folic acid content in foods containing corn masa flour if fortified at a level of 140 ug folic acid/100 g corn masa flour. **Results:** Had corn masa flour fortification occurred, we estimated that Mexican American women aged 15-44 y could have increased their total usual daily folic acid intake by 19.9% and non-Hispanic white women by 4.2%. Among the US population, estimated relative percentage increases in total usual daily folic acid intake with corn masa flour fortification were greatest among Mexican Americans (16.8%) and lowest among children aged 1-3 y (2%) and adults aged >51 y (0-0.5%). **Conclusion:** Analyses suggest that corn masa flour fortification would have effectively targeted Mexican Americans, specifically, Mexican American women, without substantially increasing folic acid intake among other segments of the population. Such increases could reduce the disparity in total folic acid intake between Mexican American and non-Hispanic white women of childbearing age and implies that an additional NTD preventive benefit would be observed for Mexican American women.

Keywords

folic acid, corn, flour, food composition, health survey, Hispanic, information processing, neural tube defect, population, pregnancy, vitamin intake, dietary supplements, neural tube defects, nutrition surveys, preconception care, vitamin B complex, Zea mays

Disciplines

Biochemical Phenomena, Metabolism, and Nutrition | Public Health | Statistics and Probability

Comments

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ABSTRACT

Background: Folic acid can prevent up to 70% of neural tube defects (NTDs) if taken before pregnancy. Compared with other race-ethnicities, Hispanic women have higher rates of NTDs, lower rates of folic acid supplement use, and lower total folic acid intakes.

Objective: The objective was to assess potential effects of fortifying corn masa flour with folic acid on Mexican American women and other segments of the US population.

Design: A model was developed by using data from the National Health and Nutrition Examination Survey 2001–2004 to estimate the folic acid content in foods containing corn masa flour if fortified at a level of 140 μg folic acid/100 g corn masa flour.

Results: Had corn masa flour fortification occurred, we estimated that Mexican American women aged 15–44 y could have increased their total usual daily folic acid intake by 19.9% and non-Hispanic white women by 4.2%. Among the US population, estimated relative percentage increases in total usual daily folic acid intake with corn masa flour fortification were greatest among Mexican Americans (16.8%) and lowest among children aged 1–3 y (2%) and adults aged >51 y (0–0.5%).

Conclusion: Analyses suggest that corn masa flour fortification would have effectively targeted Mexican Americans, specifically, Mexican American women, without substantially increasing folic acid intake among other segments of the population. Such increases could reduce the disparity in total folic acid intake between Mexican American and non-Hispanic white women of childbearing age and implies that an additional NTD preventive benefit would be observed for Mexican American women. *Am J Clin Nutr* 2009; 89:305–15.

INTRODUCTION

Neural tube birth defects (NTDs) are serious birth defects of the brain (anencephaly) and the spine (spina bifida) that occur early in embryogenesis (1). Although infants born with anencephaly die shortly after birth, infants born with spina bifida can lead full and productive lives, albeit often with serious disabilities. Research has shown that folic acid, a water-soluble B vitamin, can prevent $\leq 70\%$ of folic acid-preventable NTDs when taken before and during early pregnancy (2–4). In 1992, the US Public Health Service issued a recommendation that all

women capable of becoming pregnant consume 400 μg folic acid/d to reduce the risk of having a child born with an NTD (5). This recommendation was followed by a US Food and Drug Administration (FDA) mandate to fortify enriched cereal grain products, starting in 1998, with folic acid at 140 μg /100 g flour (6). It was estimated that this level of fortification would provide on average an additional ≈ 100 μg folic acid/d (7–9). Indeed, dietary data analysis from the National Health and Nutrition Examination Survey (NHANES) 2001–2002 indicated that women of reproductive age reported receiving on average an additional 128 μg folic acid from fortified foods (10). In 1998, the Institute of Medicine published a review of data current at that time on folic acid and recommended that all women capable of becoming pregnant should consume 400 μg folic acid/d from fortified foods and supplements, or both, in addition to consuming a diet high in folate-rich foods (11).

According to surveillance systems with prenatal ascertainment during the period 1999–2000, ≈ 3020 pregnancies were affected each year by an NTD in the United States, with a total of 1640 infants born with spina bifida and 1380 infants born with anencephaly (12). There were racial-ethnic disparities in the rates of NTDs; Hispanic women had higher rates than other race-ethnicities. Williams et al (13) noted that, before fortification, Hispanic women had a prevalence rate of 10.34 births affected by NTDs per 10,000 births compared with 7.92/10,000 births for non-Hispanic white women. These rates decreased significantly after fortification (Hispanic women: 7.02/10,000;

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² The findings and conclusions in this report are those of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention.

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non-Hispanic white women: 5.35/10,000); however, the racial-ethnic differences remained (13). In addition to the differences in rates of NTD prevalence, Yang et al (10) found differences in folic acid consumption, with a lower proportion of Hispanic women consuming ≥ 400 μg folic acid from fortified foods and supplements than non-Hispanic white women. This was consistent with other findings indicating that Hispanic women were the least likely to report awareness of folic acid and consumption of supplements containing folic acid (14).

Because of the persistence of the racial-ethnic differences in NTD prevalence rates, even after fortification of enriched cereal grains with folic acid, it was hypothesized that fortification of a product that could specifically target Hispanic women might increase their overall average intake of folic acid and thus reduce their risk of NTDs. Similarly, a targeted approach might not unduly increase the average daily folic acid intake of the general population, for those segments of the population for whom the intervention was not intended (ie, males).

To address this strategy, researchers investigated whether corn masa flour, which does not have a standard of identity as developed by the FDA, could be used as a vehicle for a targeted folic acid–fortification program. Corn masa flour is a key ingredient in many traditional Latin American cuisines, including corn tortillas, enchiladas, and tamales. Corn masa flour food items are reported to be consumed in appreciable quantities in the Latin American diet, particularly among Mexicans and Central Americans (15). A model was developed to assess the potential effect of additional folic acid fortification of corn masa flour on the folic acid intakes of Mexican Americans, specifically Mexican American women, and that of the general US population.

SUBJECTS AND METHODS

NHANES 2001–2004

NHANES 2001–2004 was conducted according to a stratified multistage probability design. The survey captured a nationally representative sample of the noninstitutionalized civilian US population. Respondents participated in a household interview and a physical examination. For this analysis, we did not include individuals who were pregnant and those whose dietary interview did not meet minimum required standards for data quality (16). Additionally, analyses reported by race-ethnicity were restricted to non-Hispanic white, non-Hispanic black, and Mexican American respondents because of the small number of individuals of other racial and ethnic groups. All participants in NHANES provided written informed consent.

Modeling of folic acid intake from corn masa flour

Modeling possible folic acid intake from fortified corn masa flour entailed 4 main steps: 1) identification of foods that contained corn masa flour, 2) determination of the proportion of corn masa flour per food item, 3) determination of the amount of additional folic acid derived from corn masa flour fortified at 140 μg folic acid/100 g corn masa flour per food item, and 4) creation of model variables with the additional folic acid intake from fortified corn masa flour.

To identify foods that could contain corn masa flour, 4 researchers independently reviewed ≈ 6940 foods listed in the NHANES 2001–2004 food codes. Three of the researchers were Hispanic. Each individual's list was compared for similarities and differences in identifying foods. Foods were excluded if they contained words such as *white flour* or if the conventional product used was a white flour tortilla (eg, burritos). Foods were included in the initial list if there was a good possibility that they contained corn masa flour. The resulting list of foods was then reviewed by an international manufacturer of corn masa flour to validate whether the foods identified did indeed contain corn masa flour. Foods identified by researchers and validated by an international manufacturer of corn masa flour were included in the analyses, which resulted in 87 foods from the food code list (**Appendix A**).

To determine the proportion of corn masa flour present in each food, each food item was identified in the MyPyramid Equivalents Database for the US Department of Agriculture (USDA) Survey Food Codes, 1994–2002, version 1.0. On the basis of data from 2001 to 2002, the individual components or commodities of each food product were identified (eg, non-whole-wheat grains, vegetables, or fruit). Because this database did not specifically list corn masa flour as an individual component of food products, the non-whole-wheat grain component was used as a proxy. For most of the foods identified and analyzed, the entire grain component was listed as nonwhole grains. For purposes of this analysis, corn masa flour was considered a non-whole-grain based on its manufacturing process, called nixtamalization—a process that involves steeping dried corn in hot water and exposing it to calcium hydroxide or lime (17). This process hydrolyzes the pericarp and removes it from the grain. The aqueous solution is then drained, and the remaining nixtamal is washed several times, removing seed coats, tip caps, excess lime, and any other impurities (17, 18). It was assumed that most identified food products would use corn masa flour as the major flour or grain ingredient, thus making the non-whole-grain component a reasonable proxy.

To determine the total grams of flour in each food item, the total grain ounce equivalents, made up of both nonwhole grains and whole grains, were multiplied by 16 g. MyPyramid Equivalents Database documentation used 16 g as a standard amount of flour in 1 ounce equivalent for many of the foods in the grains group. Sixteen grams of flour is found in a slice of commercial white bread weighing 26 g. From this, the proportion of non-whole-grain grams per food item, the proxy for the amount of corn masa flour, was determined. A sample calculation follows:

Food item A

Total grain ounce equivalents: 3.5

Nonwhole grain ounce equivalents: 2.0

Whole grain ounce equivalents: 1.5

Grams of nonwhole grain: $2.0 \times 16 = 32$ g nonwhole grain in food item A

Because the proportion of nonwhole grain ounce equivalents was not available for the NHANES 2003–2004 food products, a ratio of the nonwhole grain ounce equivalents per gram of food for each food item from the MyPyramid Equivalents Database 2001–2002 data were used to determine the nonwhole grain ounce equivalents for 2003–2004 data. A sample calculation follows:

Food item B (2001–2002)

Total grams of food item: 354

Nonwhole grain ounce equivalents: 1.6

Proportion of nonwhole grain ounce equivalents per gram of food: $1.6/354 = 0.00452$

Food item B (2003–2004)

Total grams of reported food consumed in 2003–2004: 100

Proportion of nonwhole grain ounce equivalents from 2001 to 2002 per gram of food: 0.00452

Nonwhole grain ounce equivalents: $0.004527 \times 100 = 0.4527$

Grams of nonwhole grain: $0.4527 \times 16 = 7.24$ g of nonwhole grain in food item B

Folic acid fortification was simulated by adding an additional 140 μg folic acid per 100 g corn masa flour. On the basis of the preceding example, food item A would have had an additional 44.8 μg folic acid added from corn masa flour (32 g nonwhole grain \times 140 $\mu\text{g}/100$ g) and food item B in 2003–2004 would have had 10.14 μg folic acid added from corn masa flour (7.24 g nonwhole grain \times 140 $\mu\text{g}/100$ g). The total amount of folic acid an individual would have consumed with folic acid fortification of corn masa flour included the estimated or expected intake from fortified corn masa flour plus the actual reported folic acid intake from foods and supplements.

Folic acid intake from foods

Estimated intakes of folic acid in foods were obtained by using one 24-h food recall questionnaire in NHANES 2001–2002 and two 24-h food recall questionnaires for NHANES 2003–2004. The USDA Food and Nutrient Database for Dietary Studies (FNDDS) version 1.0 was used to calculate all nutrient intakes for NHANES 2001–2002, and version 2.0 was used to calculate all nutrient intakes for NHANES 2003–2004. The FNDDS is the most current database for nutrient composition of foods, including folic acid found in fortified foods. A detailed description of the FNDDS is published elsewhere (<http://www.ars.usda.gov/Services/docs.htm?docid=12089>).

Folic acid intake from supplements

During each household interview in NHANES 2001–2004, the participant was asked about his or her use of dietary supplements, including single vitamins, multivitamins, minerals, herbs, and other similar nutritional substances over the past month. The interviewer recorded the name of each product and matched it to a list of known products. After the survey, NHANES staff obtained label information for each reported supplement to determine the ingredients. A participant was classified as a user of a dietary supplement containing folic acid if he or she reported taking such a supplement at least one time during the past month. Folic acid intake was calculated for each supplement on the basis of folic acid content, the number of days a supplement was taken, and the quantity of the supplement taken per day during the previous month. The average daily folic acid intake for each supplement was calculated, and the values were totaled across all supplements taken by each participant to yield the average daily amount of supplemental folic acid consumed (10). This estimate was added to the amount of folic acid consumed from foods for each day of intake for each individual.

Statistical analysis

Analyses were conducted by using the modeled folic acid intake to determine the potential contribution fortified corn masa flour would have on folic acid intake. It has been reported that estimates of nutrient intake based on one day's worth of intake do not account for possible within-person variation (18, 19). Therefore, PC-SIDE version 1.02 (Iowa State University, Ames, IA) was used to estimate usual nutrient intakes, which takes into account both between- and within-person variation when a subsample of the population has ≥ 2 d worth of intake as in NHANES 2001–2004. In the combined 4-y sample, respondents in the 2001–2002 wave provided only 1 d of intake information, whereas almost all of those in the 2003–2004 wave provided 2 independent days of intake information. If we can assume that the day-to-day variability in intakes did not change between waves, then we can use the within-person variance estimate based on 2003–2004 information to adjust daily intakes from the entire combined sample. Detailed descriptions of this method are given elsewhere (19, 20). We used PC-SIDE to calculate the distributions (medians, percentiles, and proportions < 400 μg) of folic acid intakes for women aged 15–44 y by race-ethnicity (non-Hispanic white, non-Hispanic black, and Mexican American), age (15–24, 25–34, and 35–44 y), and among Mexican American women who reported consuming corn masa flour. A second analysis was conducted to calculate the distributions (medians and percentiles) of folic acid intakes for the total US population by sex, race-ethnicity (non-Hispanic white, non-Hispanic black, and Mexican American), and age (1–3, 4–8, 9–13, 14–18, 19–30, 31–50, 51–70, and > 70 y). Medians for total calorie intake by race-ethnicity (non-Hispanic white, non-Hispanic black, and Mexican American) were calculated by using PC-SIDE. We also used PC-SIDE to estimate the best linear unbiased predictor (BLUPS) of individual usual folic acid intakes. BLUPS were outputted for further analyses by using Complex Samples SPSS version 14.0 (SPSS Inc, Chicago, IL).

BLUPS were not Gaussian. We log-transformed BLUPS to normalize the distribution and calculated the difference in the logs of BLUPS [$\log(\text{modeled intake}) - \log(\text{actual intake})$] to estimate the predicted relative percentage changes in usual daily folic acid intake due to corn masa flour fortification. This method was used because direct comparisons of medians was difficult without a good estimate of the SE of the difference. Differences in proportions were tested by using 2-tailed *t* tests.

We used 4-y dietary weights for all analyses, as recommended by the National Center for Health Statistics at the Centers for Disease Control and Prevention (16). For analyses conducted with PC-SIDE, SEs were calculated by using a set of 60 Jackknife replicate weights. Replicate weights were calculated by using a combination of day 1 dietary weights for NHANES 2001–2002 data and day 2 dietary weights for NHANES 2003–2004.

A total of 292 participants (241 from 2001 to 2002 and 51 from 2003 to 2004) who reported consuming a supplement containing folic acid were missing information regarding the frequency of supplement use. These participants were not included as supplement users in the analyses presented. To determine whether this exclusion would have affected the results presented, a sensitivity analysis was conducted. Individuals with missing frequency data were assigned a daily intake of either 0 or 400 μg .



RESULTS

NHANES 2001–2002 selected 13,156 individuals for the sample; 11,039 were interviewed (83.9%) and 10,477 were examined in the Mobile Exam Center (79.6%). NHANES 2003–2004 selected 12,761 individuals for the sample; 10,122 were interviewed (79.3%) and 9,643 were examined in the Mobile Exam Center (75.6%). This left 20,120 individuals available for analysis of all ages. Individuals whose dietary interviews did not meet the minimum required standards for data quality for day 1 and day 2 ($n = 2,206$) and women who reported being pregnant at the time of the survey ($n = 571$) were not included in the analyses. Most of those individuals excluded for poor data quality on their dietary interview were either infants or children aged <2 y whose reported consumption of breast milk limited the ability to quantify the total caloric and nutrient intake ($n = 323$). The remaining individuals did not complete the dietary interview ($n = 1,703$) or did not have reliable dietary intake data ($n = 180$). Individuals who were excluded because of unreliable dietary intake data or who did not complete the dietary interview were evenly split by sex and fairly evenly distributed by age groups; however, more non-Hispanic whites were excluded. Finally, 2 individuals were excluded who had reported daily folic acid intakes >93 mg. This resulted in a final sample size of 17,341 individuals, of whom 49.4% were male, 70.1% were non-Hispanic white, 11.8% were non-Hispanic black, 8.7% were Mexican American, 4.7% were other Hispanic, and 4.7% were other races or ethnicities, including multiracial (weighted percentages). All ages of individuals were examined.

In addition, a separate analysis of women aged 15–44 y ($n = 3767$) was conducted. For this subset of the population, 318 women with dietary interviews who did not meet the minimum required standards for data quality and 587 pregnant women were not included. Women aged 35–44 y and non-Hispanic white women were more likely to have been excluded on the basis of their dietary interviews. This left 2,862 women aged 15–44 y for analysis. Of these women, 66.9% were non-Hispanic white, 13.4% were non-Hispanic black, 9.4% were Mexican American, 5.4% were other Hispanic, and 4.8% were other races or ethnicities, including multiracial (weighted percentages).

Demographics characteristics of the analytic sample by race-ethnicity are shown in **Table 1**. Supplement use was a factor in

determining overall folic acid intake. Of women aged 15–44 y, 30% reported consuming a supplement containing folic acid. Non-Hispanic white women were more likely to have reported use (37%) than were Mexican American women (21%; $P < 0.001$) and non-Hispanic black women (15%; $P < 0.001$). Within the overall population analyzed, $\approx 33\%$ of individuals reported any use of supplements containing folic acid. Non-Hispanic whites were the most likely to have taken supplements, followed by Mexican Americans and non-Hispanic blacks (38%, 19%, and 18%, respectively; $P < 0.001$). Females were more likely to have reported supplement use than were males (36% vs. 30%; $P < 0.001$) (data not shown).

More than 25% of women aged 15–44 y reported consuming corn masa flour (28%) on either day 1 or day 2 of the survey. Of these women, more Mexican American women (60%) than non-Hispanic black women (27%; $P < 0.001$) or non-Hispanic white women (23%; $P < 0.001$) reported consuming corn masa flour. Within the total US population, 56% of Mexican Americans reported consuming products identified as containing corn masa flour on either day 1 or day 2 of the survey compared with only 22% of non-Hispanic whites ($P < 0.001$) and 21% of non-Hispanic blacks ($P < 0.001$). There were no differences in intake by sex, and 4–30-y-olds were more likely to have reported a higher consumption than were the other age groups (data not shown). Reported consumption of corn masa flour products in 2001–2002 and 2003–2004 were not significantly different (20% compared with 20%; $P = 0.776$) (data not shown). Additionally, there were no differences in reported consumption of corn masa flour products in 2003–2004 for day 1 intake compared with day 2 intake (20% compared with 18%; $P = 0.092$) (data not shown).

Usual calorie intake did not differ by race-ethnicity among women aged 15–44 y. Similarly to that in women, usual calorie intake did not differ by race-ethnicity within the total US population.

The total usual daily folic acid intake for US women aged 15–44 y by race-ethnicity and age from all fortified foods and supplements compared with the modeled intake with the addition of folic acid fortified corn masa flour products for 2001–2004 is shown in **Table 2**. The usual median daily intake for women aged 15–44 y was 250 μg and in the model increased to 262 μg

TABLE 1

Characteristics of analytic sample by race-ethnicity: National Health and Nutrition Examination Survey 2001–2004¹

	Total	Non-Hispanic white	Non-Hispanic black	Mexican American
Women aged 15–44 y				
Sample size (n)	2862	1149	737	756
Reported folic acid supplement use (%)	30 (27, 34)	37 (32, 42)	15 (10, 22) ²	21 (16, 26) ²
Reported consumption of corn masa flour (%) ³	28 (24, 31)	23 (20, 27) ⁴	27 (21, 32) ⁴	60 (53, 67)
Usual calorie intake (kcal)	1950 (1884, 2016)	1971 (1886, 2056)	1958 (1824, 2092)	1987 (1879, 2095)
US population				
Sample size (n)	17,341	7203	4375	4389
Reported folic acid supplement use (%)	33 (31, 35)	38 (35, 41)	18 (15, 20) ²	19 (17, 22) ²
Reported consumption of corn masa flour (%) ³	25 (23, 27)	22 (20, 24) ⁴	21 (19, 23) ⁴	56 (52, 61)
Usual calorie intake (kcal)	2059 (2034, 2084)	2075 (2024, 2126)	2010 (1936, 2084)	2093 (2034, 2152)

¹ Race-ethnicity subanalyses were restricted to non-Hispanic whites, non-Hispanic blacks, and Mexican Americans. 95% CIs in parentheses.

² Significantly different from Non-Hispanic whites, $P < 0.001$.

³ Reported consumption of corn masa flour on either day 1 or day 2 of the survey.

⁴ Significantly different from Mexican Americans, $P < 0.001$.

with corn masa flour fortification—a 3.9% relative increase. On the basis of the model, corn masa flour fortification resulted in an estimated increase in the median usual daily intake within each racial-ethnic group. Mexican American women had a 19.9% relative increase in usual daily intake from actual to modeled (from 212 to 253 μg) compared with a 4.2% ($P < 0.001$ compared with Mexican Americans) and 5.3% ($P < 0.001$ compared with Mexican Americans) relative increase from actual to modeled for non-Hispanic white (from 273 to 285 μg) and non-Hispanic black (from 175 to 185 μg) women, respectively. With corn masa flour fortification, Mexican American women had modeled median usual daily intakes that were much closer to those reported by non-Hispanic white women, despite the higher prevalence of supplement use among non-Hispanic white women. Women aged 15–24 (5.8%) and women aged 25–34 y (4.3%) had a slightly larger relative percentage increases than did women aged 35–44 y (1.3%) ($P < 0.001$ for both). See **Appendix B** for the 25th, 50th, and 75th percentiles of usual daily intakes for women aged 15–44 y before and after corn masa flour fortification modeling.

The proportion of women consuming $<400 \mu\text{g}$ was 73% (actual) and was estimated to decrease to 71% with corn masa flour fortification (modeled). On the basis of modeling, Mexican American women had the largest decrease in the proportion of women consuming $<400 \mu\text{g}$ (85–78%) after corn masa flour fortification.

The distribution of the total usual daily folic acid intake from all fortified foods and supplements compared with the modeled intake with the addition of folic acid fortified corn masa flour products for women aged 15–44 y by race-ethnicity is shown in **Figure 1**. Almost no change in folic acid intake from actual to modeled values was observed for non-Hispanic white and non-Hispanic black women (Figure 1A and 1B); however, an increase in the distribution of Mexican American women's usual daily folic acid intake after corn masa flour fortification was observed (Figure 1C).

The total usual daily folic acid intake for the US population by sex, race-ethnicity, and age from all fortified foods and supplements compared with the modeled intake with the addition of folic acid fortified corn masa flour products for 2001–2004 is shown in **Table 3**. The median usual daily folic acid intake was 272 μg . With corn masa flour fortification, the median usual daily intake was estimated at 285 μg —a 3.2% relative increase. The relative percentage increase in folic acid intake varied slightly by sex (3.6% for males and 2.7% for females; $P = 0.006$), but varied more significantly by race-ethnicity. A reported 16.8% relative increase in the usual daily folic acid intake for Mexican Americans from actual to modeled (from 226 to 264 μg) was substantially higher than that seen for both non-Hispanic whites (4.0%; $P < 0.001$) and non-Hispanic blacks (3.6%; $P < 0.001$). All age groups saw relative percentage increases in total folic acid consumption with corn masa flour fortification. The smallest relative percentage increases were among children aged 1–3 y (2.0%) and adults aged >51 y (0–0.5%). The largest relative percentage increases were among those aged 9–30 y, ranging from 4.1% to 5.5%. See **Appendix C** for the 25th, 50th, and 75th percentiles of usual daily intakes for the total US population before and after corn masa flour fortification modeling.

An analysis of the population who reported consumption of corn masa flour on either day 1 or day 2 of the survey indicated that, among Mexican American women aged 15–44 y ($n = 453$), the median daily intake of folic acid was 218 μg (95% CI: 183 μg , 253 μg). If corn masa flour had been fortified, intakes could have increased to 290 μg (95% CI: 242 μg , 338 μg)—a 33.9% increase (95% CI: 29.5%, 38.4%) (data not shown).

A sensitivity analysis was conducted to determine whether the exclusion of participants with missing supplement frequency data could have any effect on the results. Supplement users with missing frequency data were given a value of either 0 μg daily folic acid intake from supplements or 400 μg daily folic acid intake from supplements. Data indicated that there was no

TABLE 2

Median total usual folic acid intakes and proportion of women who would consume $<400 \mu\text{g}/\text{d}$ with (modeled) and without (actual) folic acid fortification of corn masa flour among nonpregnant women aged 15–44 y by race-ethnicity and age: National Health and Nutrition Examination Survey 2001–2004¹

	Women aged 15–44 y				
	50th Percentile (95% CI)			Percentage $<400 \mu\text{g}$ (95% CI)	
	Actual usual intake	Modeled usual intake	Relative percentage change ²	Actual usual intake	Modeled usual intake
	$\mu\text{g}/\text{d}$	$\mu\text{g}/\text{d}$	%	%	%
Total ($n = 2862$)	250 (223, 277)	262 (234, 290)	3.9 (2.9, 4.9)	73 (68, 78)	71 (65, 77)
Race-ethnicity ³					
Non-Hispanic white ($n = 1149$)	273 (204, 342)	285 (242, 328)	4.2 (3.2, 5.2) ⁴	67 (58, 76)	65 (58, 73)
Non-Hispanic black ($n = 737$)	175 (155, 195)	185 (164, 206)	5.3 (4.0, 6.6) ⁴	89 (86, 92)	88 (84, 92)
Mexican American ($n = 756$)	212 (180, 244)	253 (215, 291)	19.9 (15.4, 24.5)	85 (78, 91)	78 (70, 86)
Age group					
15–24 y ($n = 1529$)	232 (208, 256)	248 (222, 274)	5.8 (4.5, 7.1) ⁵	81 (74, 87)	78 (72, 85)
25–34 y ($n = 604$)	256 (213, 299)	269 (225, 313)	4.3 (2.5, 6.1) ⁵	69 (63, 76)	67 (61, 74)
35–44 y ($n = 729$)	254 (200, 308)	263 (198, 328)	1.3 (0.3, 2.4)	68 (58, 79)	67 (56, 79)

¹ Usual intakes have taken into account both within- and between-person variation.

² The relative percentage change is the antilog of the log of modeled individual usual intakes minus the log of the actual individual usual intakes.

³ Race-ethnicity subanalyses were restricted to non-Hispanic whites, non-Hispanic blacks, and Mexican Americans.

⁴ Significantly different from Mexican Americans, $P < 0.001$.

⁵ Significantly different from women aged 35–44 y, $P < 0.001$.



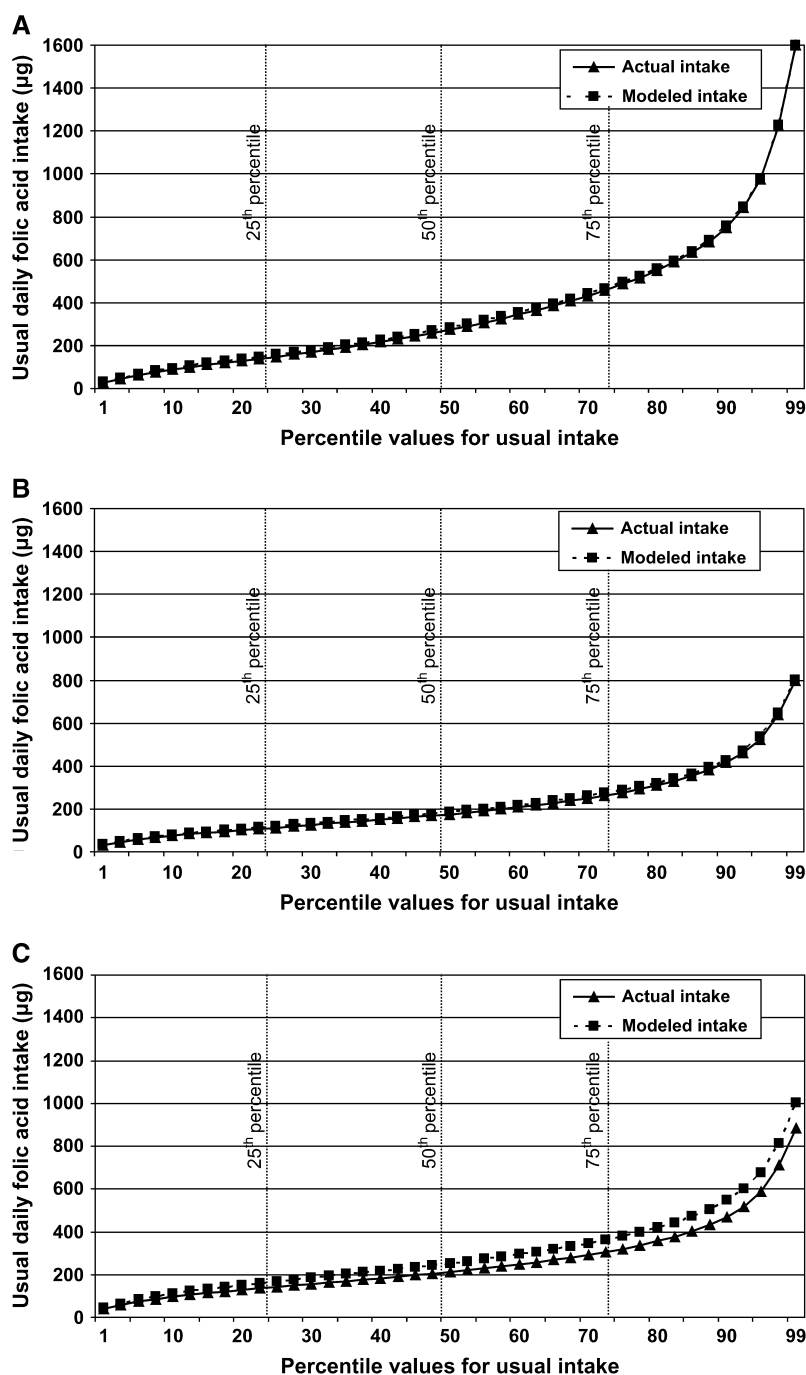


FIGURE 1. Total usual folic acid intakes with (modeled) and without (actual) folic acid fortification of corn masa flour for non-Hispanic white women (A), non-Hispanic black women (B), and Mexican American women (C) aged 15–44 y.

difference in the results when missing values were given a value of either 0 or 400 μg . This showed that the exclusion of individuals with missing supplement frequency data would not have altered the results significantly. Therefore, these individuals were excluded in the analyses presented.

DISCUSSION

Corn masa flour fortification modeling predicted that the overall usual folic acid intake of Mexican Americans, specifically, Mexican American women, was increased by this type of

fortification effort. The results suggest that Mexican American women aged 15–44 y increased their usual daily folic acid intake by 19.9%, and fewer Mexican American women would be consuming less than the daily recommended intake of 400 μg . For Mexican American women who reported consuming corn masa flour on either day 1 or day 2 of the survey, this relative percentage increase in usual daily folic acid intake could have been as high as 33.9%. The disparity between usual daily folic acid intakes among non-Hispanic white and Mexican American women also could have been reduced, despite the higher reported use of supplements containing folic acid among non-Hispanic



TABLE 3

Median total usual folic acid intakes with (modeled) and without (actual) folic acid fortification of corn masa flour for the US population by sex, race-ethnicity, and age: National Health and Nutrition Examination Survey 2001–2004¹

	50th Percentile (95% CI)		Relative percentage change ²
	Actual usual intake	Modeled usual intake	
	$\mu\text{g/d}$		%
Total (<i>n</i> = 17,341)	272 (259, 285)	285 (271, 299)	3.2 (2.8, 3.7)
Sex			
Males (<i>n</i> = 8683)	289 (277, 301)	303 (291, 315)	3.6 (3.2, 4.0)
Females (<i>n</i> = 8658)	256 (239, 273)	269 (250, 288)	2.7 (2.2, 3.3) ³
Race-ethnicity ⁴			
Non-Hispanic white (<i>n</i> = 7203)	296 (269, 323)	306 (281, 331)	4.0 (3.6, 4.4) ⁵
Non-Hispanic black (<i>n</i> = 4375)	203 (185, 221)	212 (196, 228)	3.6 (3.1, 4.0) ⁵
Mexican American (<i>n</i> = 4389)	226 (213, 239)	264 (249, 279)	16.8 (14.9, 18.7)
Age group			
1–3 y (<i>n</i> = 2114)	165 (157, 173)	169 (161, 177)	2.0 (1.6, 2.3) ⁶
4–8 y (<i>n</i> = 1646)	309 (278, 340)	320 (288, 352)	2.7 (2.3, 3.2) ⁶
9–13 y (<i>n</i> = 2101)	278 (253, 303)	292 (266, 318)	4.8 (4.1, 5.6)
14–18 y (<i>n</i> = 2629)	260 (240, 280)	274 (254, 294)	4.1 (3.4, 4.8) ⁶
19–30 y (<i>n</i> = 1955)	263 (246, 280)	283 (265, 301)	5.5 (4.5, 6.4)
31–50 y (<i>n</i> = 2813)	269 (235, 303)	287 (209, 365)	3.4 (2.5, 4.3) ⁶
51–70 y (<i>n</i> = 2468)	318 (284, 352)	327 (294, 360)	0.5 (0, 1.0) ⁶
>70 y (<i>n</i> = 1615)	322 (280, 364)	325 (284, 366)	0 (0, 0.2) ⁶

¹ Usual intakes have taken into account both within- and between-person variation.

² The relative percentage change is the antilog of the log of modeled individual usual intakes minus the log of the actual individual usual intakes.

³ Significantly different from men, *P* < 0.006.

⁴ Race-ethnicity subanalyses were restricted to non-Hispanic whites, non-Hispanic blacks, and Mexican Americans.

⁵ Significantly different from Mexican Americans, *P* < 0.001.

⁶ Significantly different from 19- to 30-y-olds, *P* < 0.001.

white women. Consuming 400 μg folic acid alone has been shown to reduce the risk of NTDs (4). A positive shift in the distribution of folic acid intake by fortifying corn masa flour could provide significant public health benefits, with a specific emphasis on the health of pregnancies among Mexican American women.

Food fortification is a long-standing public health intervention that affects a large number of people without requiring specific behavior changes. US folic acid fortification of enriched cereal grain products is credited with an increase in red blood cell folate concentrations and a 26% decrease in the prevalence of NTDs within the United States (12, 21). Some research has also indicated that folic acid might play a role in reducing the risk of other diseases or conditions, such as other birth defects (22, 23), some cancers, cardiovascular disease, and stroke (24–26); however, more research is needed to know for sure. Along with these benefits, concerns have also been raised about the potential for adverse effects of high levels of folic acid, such as the exacerbation of neurologic effects from exposure to very high doses of folic acid (11), increased risks of certain cancers (27), and cognitive decline (28, 29). Given the possible wide range of effects that folic acid might have on different segments of the population, it is not surprising that additional folic acid fortification efforts to reduce NTDs should now address how other subgroups of the population would be affected. Whether a corn masa flour fortification program could effectively target the Mexican American population, specifically Mexican American women, and the effect of corn masa flour fortification on other segments of the US population are discussed below.

Fortification, as an intervention, has been found to be effective at reaching a wide range of individuals regardless of income, educational level, or region (30). Fortification efforts can also be targeted to very specific populations by focusing on food products uniquely consumed by specific population subgroups (31). Our results suggest that Mexican Americans appeared to be targeted more effectively by corn masa flour fortification than did other race-ethnicities. Specifically, the median usual daily intake of folic acid by Mexican American women would be much closer to that of non-Hispanic white women. Nevertheless, with corn masa flour fortification, the median usual daily intake for Mexican American women would still be below the recommended 400 μg of folic acid. Mexican American women aged 15–44 y have a higher rate of NTDs (13), and some evidence suggests that specific genotypes more common among Mexican Americans might necessitate additional folic acid intake above 400 μg to prevent NTDs (32–36). Whether a 19.9–33.9% relative increase in the median usual daily intake of folic acid would shift the entire distribution and provide substantial protection to Mexican American women merits further investigation.

The entire US population saw a shift to the right in its median usual daily folic acid intake. This was seen more markedly among Mexican Americans (16.8%) than among non-Hispanic whites (4.0%) and non-Hispanic blacks (3.6%) or within age groups (ranging from 0% to 5.5%) (Table 3). This suggests that corn masa flour fortification could increase the median usual daily intake of folic acid among Mexican Americans and would not appear to substantially affect other segments of the population.



This study had several limitations. The USDA FNDDS does not categorize foods by individual food commodities (eg, corn masa flour, white flour, oil, cheese, and milk); therefore, we had to identify foods that could possibly contain corn masa flour. To address possible imprecision, researchers independently reviewed the complete list of food products and validated it with an international manufacturer of corn masa flour. The proportion of corn masa flour in each food product was obtained by a USDA data set (MyPyramid Equivalents Database), which reported the equivalents of different food groups (ie, grains groups and fruit groups) within each food product. Corn masa flour was not specifically identified in the database; however, it was assumed that most of the grain used in each product would be corn masa flour. If there were other flours used in the food products, such as white or whole-wheat flour, the analyses would have overestimated the proportion of corn masa flour in each product and the potential intake of folic acid from the fortified corn masa flour.

Reported consumption of corn masa flour on either day 1 or day 2 of the survey was 56% among all Mexican Americans and 28% among all women aged 15–44 y. Although these percentages suggest a moderate consumption of corn masa flour in the United States, other data suggest that corn masa flour consumption is and continues to be a large component of the diet among Hispanics in the United States. A study that assessed the sources of nutrient intakes among low-income Hispanic women and children found that 29.4% of women and 21% of children reported consuming corn tortillas (which are made from corn masa flour) based on a 24-h recall (37). This estimate was much lower than our estimate for Mexican American women consuming corn masa flour products (60%), most likely because our definition of corn masa flour products included more than just corn tortillas. Data from the USDA's Economic Research Service indicated that US per capita consumption of corn flour and meal has increased by 178%, compared with only 32% for wheat flour, during the period 1970–2000 (38). Additionally, research has suggested that corn masa flour is widely consumed among Mexicans and Central Americans (15, 39, 40). Based on the increase in per capita consumption of corn flour and meal in the United States (38) and the documented high level of consumption of corn masa flour among Hispanics (15, 39, 40), the proportion of the population exposed to corn masa flour, especially among the Hispanic population, will remain fairly high within the United States.

NHANES 2001–2002 and NHANES 2003–2004 used the most current version of the FNDDS to analyze the nutrient content of foods; however, 2 different versions were used for the analysis (version 1 for 2001–2002 and version 2 for 2003–2004). Data from the 2001–2002 and 2003–2004 periods were analyzed separately to determine whether there were any significant differences between data for these periods. Although the 2 versions of the FNDDS did not appear to affect the analysis, there was not an independent validation or comparison of the accuracy of the estimated intakes for folic acid. The analysis used the appropriate and most up-to-date version of the FNDDS; however, new products are always entering the market, making the food-composition database difficult to keep updated (41, 42). This could have resulted in missing new products or coding new products as products that no longer existed, which could have misrepresented the nutrient intake of the US population. Additionally, analyses are based on the level of folic acid reported in

FNDDS. It has been suggested that the actual amount of folic acid in foods could differ from what is allowed by the FDA and lead to an underestimation of folic acid intake (43–45). Dietary folic intake data used in the analysis were collected by using 24-h recalls, which are subject to systematic underreporting (46). However, the differential effect of this underreporting on specific food components and on population subgroups is not well understood. Nonetheless, these analyses showed no differences in reported total usual energy intake by race-ethnicity, which suggests that if a bias were present, it was not limited to one race-ethnic group. Additionally, daily folic acid supplement intake was calculated by using an indirect method that assumed that use over 1 mo could be applied to two 24-h recalls. This calculation might not represent daily amounts for persons who do not take supplements consistently.

Healthy People 2010 objective 16–16a promotes an increase in the number of women of childbearing age who report consuming 400 μg folic acid/d to 80% to reduce their risk of NTDs (47). On the basis of modeling, Mexican American women can increase their folic acid intake by consuming fortified corn masa flour products. Nevertheless, the median usual daily folic acid intake for Mexican American women aged 15–44 y remains well below the recommended 400 μg folic acid/d, even with corn masa flour fortification. However, the addition of fortified corn masa flour could cause a small upward shift in overall usual median consumption of folic acid for the entire US population and a larger upward shift among Mexican American women. The shift in folic acid intake among Mexican American women would reduce the disparity of folic acid intake between Mexican American and non-Hispanic white women. Although it is difficult to estimate the exact benefit that corn masa flour fortification could have on the prevalence of NTDs among Mexican American women, the increased consumption of folic acid would shift some women to a level of protection not apparent without corn masa flour fortification.

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APPENDIX A

From National Health and Nutrition Examination Survey 2001–2004 food codes: foods considered to contain corn masa flour¹

Tortilla, corn	Tamale with meat and/or poultry (includes tamale, NFS)
Taco shell, corn	Tamale, meatless, Caribbean or Puerto Rican style
Salty snacks, corn/cornmeal base, nut/nug, toasted	Tamale, plain, meatless, no sauce, Mexican
Salty snacks, corn or cornmeal, corn chips, and cheese	Tamale casserole with meat
Salty snacks, corn or cornmeal, corn puffs, and twists	Tamale casserole, PR (tamales en cazuela)
Salty snacks, corn or cornmeal, and tortilla chips	Tamale in a leaf, PR (tamales en hoja)
Salty snacks, corn/corn-cheese chips, unsalted	Tamale, sweet
Salty snacks, corn/cornmeal base, tortilla chips light	Tamale, sweet, with fruit
Salty snacks, tortilla chips, fat free, with oleo	Pupusa, cheese-filled
Salty snacks, corn/cornmeal base, tortilla, low-fat, baked	Pupusa, meat-filled
Salty snacks, corn/cornmeal, tortilla, low-fat, baked, no salt	Chalupa with beans, cheese, lettuce, and tomato
Salty snacks, corn/cornmeal base, with oat bran, tortilla chips	Chalupa with beef, cheese, lettuce, tomato, and sour cream
Salty snacks, corn-based/cheese puffs and twists, low-fat	Chalupa with beef, cheese, lettuce, tomato, and salsa
Tortilla chips, unsalted	Chalupa with beans, chicken, and cheese
Nachos with beef, beans, cheese, and sour cream	Chalupa with chicken, cheese, lettuce, tomato, and sour cream
Nachos with cheese and sour cream	Chalupa with chicken, cheese, lettuce, tomato, and salsa
Nachos with cheese, meatless, no beans	Gordita/sope shell, plain no filling, grilled, no fat added
Nachos with beans, no cheese	Gordita/sope shell, plain, no filling, fried in oil
Nachos with beans and cheese	Quesadilla with cheese, meatless
Nachos with beef, beans, and cheese	Quesadilla with meat and cheese
Nachos with beef and cheese	Taco/tostada with beef, cheese, and lettuce
Nachos with chili	Taco or tostada with beef, lettuce, tomato, and salsa
Nachos with beef, beans, cheese, tomatoes, and onions	Taco/tostada with beef, cheese, lettuce, tomato, and salsa
Nachos with chicken/turkey and cheese	Taco with beef, cheese, lettuce, tomato, and sour cream
Enchilada with beef, no beans	Soft taco with beef, cheese, and lettuce (includes Taco Bell)
Enchilada with beef and beans (include enchilada, NFS)	Soft taco with chicken, cheese, and lettuce
Enchilada with beef, beans, and cheese	Soft taco with chicken, cheese, lettuce, tomato, and sour cream
Enchilada with beef and cheese, no beans	Taco/tostada with chicken/turkey, lettuce, tomato, and salsa
Enchilada with ham and cheese, with no beans	Taco/tostada with chicken, cheese, lettuce, tomato, and salsa
Enchilada with chicken, tomato-base sauce	Soft taco with beef, cheese, lettuce, tomato, and salsa
Enchilada with chicken and beans, tomato-base sauce	Taco or tostada with fish
Enchilada with chicken, beans, cheese, and tomato sauce	Taco/tostada with beans, meatless, lettuce, tomato, and salsa
Enchilada with chicken and cheese, no beans, and tomato sauce	Taco/tostada with beans, cheese, lettuce, tomato, and salsa
Enchilada with beans, meatless	Taco or tostada with beans, cheese, meat, lettuce, tomato, and salsa
Enchilada with beans and cheese, meatless	Taco salad with beef and cheese, corn chips
Enchilada with cheese, meatless, no beans	Flauta, NFS
Enchilada with seafood, tomato sauce	Flauta with beef
Beef enchilada dinner, NFS (frozen meal)	Flauta with chicken
Beef enchilada, gravy, rice, and refried beans (frozen)	Taquitos
Cheese enchilada with beans and rice (frozen meal)	Taco with crab meat, PR (tacos de jueyes)
Cheese enchilada (frozen meal)	
Chicken enchilada (diet frozen meal)	
Chicken enchilada with salsa, rice, vegetables, des (diet frozen)	
Chilaquiles, tortilla casserole with salsa, cheese, and egg	
Chilaquiles, tortilla casserole, and no egg	
Pochito (frankfurter/hot dog and beef chili in tortilla)	
Huevos rancheros	

¹ NFS, not further specified; PR, Puerto Rican.

APPENDIX B

Total usual folic acid intakes with (modeled) and without (actual) folic acid fortification of corn masa flour for nonpregnant women aged 15–44 y by race-ethnicity and age: National Health and Nutrition Examination Survey 2001–2004¹

	Women aged 15–44 y					
	Usual intake			Modeled usual intake		
	25th Percentile	50th Percentile	75th Percentile	25th Percentile	50th Percentile	75th Percentile
Total (n = 2862)	148	$\mu\text{g/d}$ 250	419	158	$\mu\text{g/d}$ 262	438
Race-ethnicity ²						
Non-Hispanic white (n = 1149)	148	273	486	158	285	495
Non-Hispanic black (n = 737)	113	175	276	121	185	288
Mexican American (n = 756)	142	212	320	169	253	379
Age group						
15–24 y (n = 1529)	148	232	356	161	248	375
25–34 y (n = 604)	141	256	465	150	269	483
35–44 y (n = 729)	147	254	476	153	263	489

¹ Usual intakes have taken into account both within- and between-person variation.

² Race-ethnicity subanalyses were restricted to non-Hispanic whites, non-Hispanic blacks, and Mexican Americans.

APPENDIX C

Total usual folic acid intakes with (modeled) and without (actual) folic acid fortification of corn masa flour for the US population by sex, race-ethnicity, and age: National Health and Nutrition Examination Survey 2001–2004¹

	US population					
	Usual intake			Modeled usual intake		
	25th Percentile	50th Percentile	75th Percentile	25th Percentile	50th Percentile	75th Percentile
Total (n = 17,341)	159	$\mu\text{g/d}$ 272	455	168	$\mu\text{g/d}$ 285	469
Sex						
Males (n = 8683)	174	289	462	184	303	479
Females (n = 8658)	147	256	446	154	269	456
Race-ethnicity ²						
Non-Hispanic white (n = 7203)	160	296	501	169	306	509
Non-Hispanic black (n = 4375)	132	203	322	137	212	333
Mexican American (n = 4389)	151	226	343	173	264	399
Age group						
1–3 y (n = 2114)	110	165	254	112	169	260
4–8 y (n = 1646)	210	309	445	219	320	456
9–13 y (n = 2101)	196	278	385	209	292	402
14–18 y (n = 2629)	171	260	388	182	274	405
19–30 y (n = 1955)	163	263	418	177	283	440
31–50 y (n = 2813)	157	269	461	165	287	477
51–70 y (n = 2468)	148	318	527	154	327	532
>70 y (n = 1615)	147	322	524	150	325	526

¹ Usual intakes have taken into account both within- and between-person variation.

² Race-ethnicity subanalyses were restricted to non-Hispanic whites, non-Hispanic blacks, and Mexican Americans.

